UNIT FIVE OUTLINE OF LESSON

INDUCED PLURIPOTENT STEM CELLS

CA Science Standards

Biology/Life Sciences

1. d. *Students know* the central dogma of molecular biology outlines the flow of information from transcription of ribonucleic acid (RNA) in the nucleus to translation of proteins on ribosomes in the cytoplasm.
4. c. *Students know* how mutations in the DNA sequence of a gene may or may not affect the expression of the gene or the sequence of amino acids in an encoded protein.
4. d. *Students know* specialization of cells in multicellular organisms is usually due to different patterns of gene expression rather than to differences of the genes themselves.
5. c. *Students know* how genetic engineering (biotechnology) is used to produce novel biomedical and agricultural products.
5. d.* *Students know* how basic DNA technology (restriction digestion by endonucleases, gel electrophoresis, ligation, and transformation) is used to construct recombinant DNA molecules.
5. e.* *Students know* how exogenous DNA can be inserted into bacterial cells to alter their genetic makeup and support expression of new protein products.

Goals/Objectives

1. Distinguish among multipotent, pluripotent, and totipotent stem cells-review

2. Explain the advantages and disadvantages of iPS cells compared to embryonic stem cells.

3. Describe the various methods for creating iPS cells, including transfection methods using plasmids; retroviruses; small molecules; and adenoviruses, and discuss the advantages and disadvantages of each.

4. Describe issues that must be resolved before these cells can safely be used in human cell based therapy.

NOTE: Prior to teaching this unit students should have a basic understanding of embryonic stem cells. Teaching the IVF lesson or the PowerPoint introductory presentation should be sufficient. This lesson is intended for advanced or AP biology students.

Outline of Unit:

I. Invitation

A. Watch Nova Science Now documentary on induced Pluripotent Stem Cells. 14:00. http://www.pbs.org/wgbh/nova/sciencenow/0305/03.html (NSN_StemCells). Students record responses on the Unit 5 NOVA Science Now Question Sheet.
   a. Download student version here
   b. Download teach version here

B. Discuss questions from the guided lecture worksheet in group discussion. (NOVA ScienceNow questions)

C. Review basic stem cell biology by watching animation and completing the Unit 5 Stem Cell Basics Worksheet. Download worksheet here.

II. Exploration

A. Lecture-Introduction to iPS technology. See Teacher Background Information in Brief Outline of Unit Five. Also refer to the paper, A Brief History of iPSCell Research.

1. Review how embryonic stem cells are made
2. Discuss pluripotency
3. Summarize iPS technology

B. Discuss, in class, the summary of the research paper that describes iPS (Yamanaka 2006 Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors). Before moving on to the jigsaw study below, students should understand the following:

1. What are the Four Transcription Factors that are used in iPS creation?
2. How do they make somatic cells turn into embryonic stem cell-like cells?
3. What transfection method did the researchers use?
4. How did the researchers detect cells that had turned into iPS cells?
5. How did the researchers test whether the iPS cells were pluripotent or not?
6. How efficient was this technique?

C. The Promises and Risks of iPS cells. A jigsaw study of summaries of iPS readings. Download Unit 5 jigsaw instructions . Download iPS readings by clicking below.

1. Yamanaka 2008 Generation of Pluripotent Stem Cells from Adult Mouse Liver and Stomach Cells-this paper demonstrates that other cell types can be used for iPS. Stomach and liver cells are more difficult to acquire, but this study indicates they are less likely to develop into cancer than skin.
   Download paper [free registration required]
   Download summary

2. Eggan 2008 iPS Generated From Patients with ALS can be Differentiated into Motor Neurons. iPS and ALS-creating diseased cells in culture from iPS cells
   Download paper [free registration required]
   Download summary

3. Jaenisch 2007 Treatment of Sickle Cell Anemia Mouse Model with iPS Cells Generated from Autologous Skin-sickle cell and a mouse model of iPS based therapy
   Download paper [free registration required]
   Download summary

4. Plath 2008 The Many Ways to Make an iPS cell-an alternative to the use of retroviruses
   Download summary

5. Yamanaka 2008 Generation of Induced Pluripotent Stem Cells without Myc from Mouse and Human Fibroblasts-iPS cells without c-Myc are transformed less efficiently but are less likely to develop cancer.
   Download summary

6. Chiang, Scientists Make Stem Cells that are Accepted by the Ethical Community
   Download paper

D. Review

1. View the Unit Five PowerPoint presentation: Human Induced Pluripotent Stem Cells. Alternatively, this ppt can be used to accompany any part of the lesson the teacher chooses.

2. Read and discuss Unit 5 "iPS Questions and Answers" .

III. Application

A. Form in-class groups to discuss the following and report back positions: List advantages and disadvantages of human embryonic stem cells compared to iPS cells in the following categories

-Ethics
-Efficiency in creation of cell lines
-*In vitro* disease models
-Safety in cell transplant therapy

B. Simulation activity

1. Several students in the class comprise an Ethical Review Board. These students do not participate in jigsaw for iPS treatment options, but instead, read up on what an ERB is and how they normally make decisions. Student groups present various treatment options to the ethical review board, which then comes to a consensus on treatment options for the patients. Ethical Review Board members give presentation on ERB background and history. They hear the arguments made for the various methods, then come to a consensus on which are safe to proceed and why.

IV. Assessment

A. Students read the following scenario and write response on essay exam. Teacher guide to question can be found in Unit Five Thalassemia paper

1. You are a doctor who wants to treat a patient for thalassemia. Thalassemia is a genetic disease caused by a mutation in hemoglobin that disrupts the molecule's ability to carry and deliver oxygen in the body. You want to try to treat your patient with iPS cells. Describe how you would obtain or produce the iPS cells. Include the original cell type and transfection method and why you have chosen these methods. Also describe how the iPS cells would be treated before transplantation.